REMARKS

Claims 28, 30, 33, 35, 36, 39, 44, 45 and 51-54 are pending and under consideration. With this Amendment, Claims 28, 30, 33, 35, 36, 39, 44, 45 and 51-54 are being canceled, without prejudice against their reintroduction into this or one or more timely filed continuation, divisional or continuation-in-part applications, and Claims 55-68 are being newly added. Thus, after entry of this Amendment, Claims 55-68 are pending and under consideration. The amendments of the claims (and specification, if warranted) and the various rejections raised in the Office Action are discussed in more detail, below.

The Amendments of the Claims

For clarity, claims 27, 29-33, 44, 46, and 48 have been cancelled and replaced with new claims 55-68. Support for new claims 55-68 is shown in Table 1. No new matter is added by virtue of the amendments.

TABLE 1

New Claim	Support (previously pending claim # and/or page:line number)
55	Claims 28 and 51
56	Claim 30
57	Claim 36
58	Claim 33
59	Claims 39 and 52
60	Claims 36 and 52
61	Claims 51 and 52
62	Claim 54

New Claim	Support (previously pending claim # and/or page:line number)
55	Claims 28 and 51
63	Claim 53
64	Claim 44
65	Claim 44
66	Claim 44
67	45
68	47

Claims 55-68 are thus presented for further examination, with

- claims 55-57 drawn to an isolated recombinant polypeptide;
- claims 59-61 drawn to an isolated recombinant fusion protein;
- claim 58 drawn to immunogenic fragments;
- claims 62-63 drawn to immunogenic compositions;
- claims 64-67 drawn to vaccine compositions; and
- claim 68 drawn to a method for inducing an immune response.

Priority

Applicant notes the Examiner's statement regarding priority document U.K. 9914945.2[1]. Applicant is still in the process of obtaining a copy of the priority document and will submit it in due course.

[1] The Office Action requests a copy of the certified priority document U.K. 9914945031.2, which Applicant assumes is GB 9914945.2.

Claim Objections

The Examiner regrets objecting to previously pending claim 47, because the amendment made to claim 47 in the previous response to office action[2] by Applicant resulted in the limitation "to a mammal" to appear twice in claim 47[3].

Previously pending claim 47 has been replaced by new claim 68, in which the limitation "to a mammal" is recited only once.

Rejection Under 35 U.S.C. § 112, first paragraph (written description)

Claims "28(b)" 33, 35, 39, 44, 45, 47 and 51-54 stand rejected under 35 U.S.C. §112, first paragraph, for the same reasons as set forth in the previous action. Specifically, the Examiner maintains that there is no written description support in the specification for fragment sequences of SEQ ID NO:2.[4] Claims "28(b)" 33, 35, 39, 44, 45, 47, and 51-54 have been cancelled[5] and replaced with new claims "55(b)" 58, 59, 64, 66, 67, and 68. Applicant traverses the rejection as it applies to new claims "55(b)" 58, 59, 64, 66, 67, and 68.

Before addressing the Examiner's specific contentions, it is worth pondering for a moment certain of the genera embraced by new claims "55(a), 56 and 57 (replacing cancelled claims "28(a)" and 30), which are acknowledged to have adequate written description support in the specification.

---

[2] Amendment under 37 C.F.R. § 1.111, mailed February 16, 2005.

[3] Office Action, page 2.

[4] Paraphrasing Office Action, page 3.

[5] Hence the rejection is moot as applied to cancelled claims "28(b)" 33, 35, 39, 44, 45, 47, and 51-54.

Claims "55(a)"[6], 56 and 57 are drawn to a genus of "isolated recombinant protein[s]," each of which contains the entire sequence set forth in SEQ ID NO:2. New claim 60, is drawn to "[a]n isolated fusion protein comprising the recombinant polypeptide of claim 56." New claim 63, is drawn to "[a]n immunogenic composition comprising the recombinant polypeptide of claim 56."

In each case, the claimed genus embraces an infinite number of recombinant species. In each case, however, the Examiner properly concludes that the genus is adequately described, recognizing that SEQ ID NO:2 is a "structural feature[] commonly possessed by members of the genus that distinguish[es] them from all others," description of which suffices to describe the genus as a whole. *Regents of the University of California v. Eli Lilly & Co.*, 119 F.3d 1559, 1568 - 69 (Fed. Cir. 1997) (holding, with respect to claims drawn to cDNAs, that a "description of a genus of cDNAs may be achieved by means of . . . a recitation of structural features common to the members of the genus, which features constitute a substantial portion of the genus.").[7]

Turning, then, to specific concerns, the Examiner contends that "the specification does not disclose an isolated recombinant polypeptide comprising an immunogenic fragment

---

[6] That is, a hypothetical claim that constructively recites:

> 55a. An isolated recombinant polypeptide comprising: the amino acid sequence of SEQ ID NO. 2.

[7] SEQ ID NO:2 is a ***structural*** recitation, not a "definition by ***function***, . . . [which] as we have previously indicated, does not suffice to define the genus because it is only an indication of what the gene does, rather than what it is. . . . " *Regents of the University of California v. Eli Lilly & Co.*, 119 F.3d 1559, 1568 (Fed. Cir. 1997) (emphasis added). SEQ ID NO:2 is a "recitation of the sequence" shared by the members of the genus, not a "mere name" which alone would not suffice. *Regents*, 119 F.3d at 1569.

comprising at least 15 amino acids or 20 amino acids of SEQ ID NO:2 . . . or an immunogenic composition comprising said fragments or fusion protein comprising said fragments. . . . "[8]

The statement is logically untenable and wrong.

The Examiner acknowledges that the specification "describes . . . an isolated recombinant polypeptide comprising the 276 amino acid sequence, SEQ ID NO:2. . . . " Office action at 3. In working examples, not credited by the Examiner, this full-length protein is expressed as a his-tagged fusion, purified, and used to prepare anti-*Moraxella* antibodies.

Description of "[a]n isolated recombinant polypeptide comprising the 276 amino acid sequence, SEQ ID NO:2" is, logically, equally the description of an isolated recombinant polypeptide comprising all possible fragments of SEQ ID NO:2. Description of an isolated recombinant fusion comprising the entire 276 amino acid sequence is, by force of logic, also the description of an isolated recombinant fusion protein comprising all possible fragments of SEQ ID NO:2. Description of an immunogenic composition comprising a his-tagged full length fusion is, logically speaking, additionally the description of an immunogenic composition comprising a protein that includes all possible immunogenic fragments of SEQ ID NO:2.

The logical infirmity of the Examiner's comment suggests that the rejection might in truth be more soundly formulated as an enablement rejection, one motivated by the Examiner's uncertainty over the routine immunogenicity of BASB111 fragments, and by the Examiner's failure to appreciate that clinical diagnosis is readily effected, without undue experimentation, using *M. catarrhalis*-specific antibodies raised against such fragments.

Such a reformulation of the rejection would rationalize the otherwise improbable statements that "the immunological function of this gene or its product in assessing Otitis media

---

[8] New claims "55(b)", 58, 59, 61, and 62 are drawn to an immunogenic fragment comprising at least 40 amino acids of SEQ ID NO:2, or an immunogenic composition comprising said fragments, or fusion protein comprising said fragments.

has not yet been identified,"[9] that "[t]he specification fails to disclose any substitution, insertion or deletion or changes have been made in a polypeptide SEQ.ID.NO:2 to obtain immunogenic fragments,"[10] and "[t]he specification does not describe any use of fragments as claimed . . . in identifying *M. catarrhalis* infection."[11] In each case, the underlying concern is directed to the immunogenicity of fragments, and the ability to use immunogenic fragments in methods of diagnosis.

Significantly, such a reformulation would also serve to harmonize the Examiner's treatment of claims drawn to an isolated recombinant protein, each of which comprises the entire sequence set forth in SEQ ID NO:2, e.g., new claims "55(a)", 56, 57, 60 and 63, the genera of which are acknowledged to be adequately described, with the assertion that

> [t]he specification . . .. does not satisfy the written description guidelines[12] because an isolated polypeptide comprising (open language) at least 15 amino acids of SEQ ID NO:2 plus unlimited and unknown amino acids and an isolated polypeptide comprising 20 amino acids of SEQ ID NO:2 plus unlimited and unknown amino acids would result in an unknown fragments [sic] without any structure and other identifying characteristics such as function.[13]

Reformulated as an enablement rejection, the Examiner's comments are seen to focus not on the "unlimited and unknown amino acids" that might **additionally** be present within the recombinant protein or fusion – such feature being equally present among the infinite number of

---

[9] The BASB111 gene does not serve an "immunological function" in *Moraxella*, a bacterium that lacks what would properly be called an immune system.

[10] The claims rejected for inadequate written description ***literally*** require SEQ ID NO:2, without ***literally*** permitting of substitution, insertion or deletion or changes.

[11] The claims are drawn to compounds and compositions, not to methods of use.

[12] Rejections, of course, are not properly founded on PTO Guidelines, but rather on the statutory provision that the Guidelines purport to interpret.

[13] Office Action, page 4.

species within the genera of claims "55(a)", 56, 57, 60 and 63 – but rather on the BASB111 portion of such recombinant proteins, with the rejection squarely predicated on a concern that the BASB111 moiety, with presumptively unpredictable immunogenicity, is thus inadequately described.

As to such concern, applicant commends the Examiner's attention to the enablement discussion below, incorporated here by reference,[14] and respectfully submits that a sufficiently high percentage of fragments of 40 or more contiguous BASB111 amino acids prove immunogenic as to allay this concern. All such fragments are present within, and being readily recognized, are fully described within, the full length sequence. Accordingly, the currently rejected claims are fully and adequately described, and the rejection, which is in error, should be withdrawn.

Rejection Under 35 U.S.C. § 112, first paragraph (scope of enablement)

Claims 28, 33, 35, 39, 44, 45, 47 and 51-54

Claims 28, 33, 35, 39, 44, 45, 47 and 51-54 stand rejected under 35 U.S.C. §112, first paragraph, for the same reasons as set forth in the previous action. Claims 28, 33, 35, 39, 44, 45, 47 and 51-54 have been cancelled[15] and replaced with new claims 55, 58, 59, 64, 66, 67, and 68. Applicant traverses the rejection as it applies to new claims 55, 58, 59, 64, 66, 67, and 68.

> Acknowledging that
>
> applicants are enabled for an immunogenic fragment consisting of 15 or 20 contiguous amino acids of SEQ.ID.NO:2, wherein the isolated polypeptide, when administered to a subject in a suitable

[14] Recognizing that applicant may have misapprehended the Examiner's intent, applicant respectfully requests a personal interview at which this, and other rejections of record, may be further explored.

[15] Hence the rejection is moot as applied to cancelled claims 28, 33, 35, 39, 44, 45, 47, and 51-54.

> composition . . . , induces an antibody or T-cell response that recognizes the polypeptide SEQ.ID.NO:2,[16]

The Examiner nonetheless contends that the specification does not provide enablement for:

> making and using fragments of a polypeptide in generating antibodies, sufficient to specifically diagnose otitis media and respiratory disease caused by Moraxella catarrhalis infections or sufficient to elicit a protective immune response against otitis media and respiratory disease caused by Moraxella catarrhalis infection.[17]

The Examiner properly does not question the ***immunogenicity*** of the BASB111 fragments themselves.

It has of course been well known for over two decades that synthetic peptides of 15 or more contiguous amino acids, when coupled to a protein carrier, are capable of eliciting antibodies to the native protein at remarkably high frequency. Niman *et al.*, "Generation of protein-reactive antibodies by short peptides is an event of high frequency: implications for the structural basis of immune recognition," *Proc. Natl. Acad. Sci. USA* 80:4949-4953 (1983) (attached hereto as Exhibit A); Shinnick *et al.*, "Synthetic Peptide Immunogens as Vaccines," *Ann. Rev. Microbiol.* 37:426-26 (1983) (attached hereto as Exhibit B); Geysen *et al.*, "Small peptides induce antibodies with a sequence and structural requirement for binding antigen comparable to antibodies raised against the native protein," *Proc. Natl. Acad. Sci. USA* 82:178-82 (1985) (attached hereto as Exhibit C).

It is also well known that such antibodies have sufficient affinity and/or avidity to prove useful in detecting pathogens. Dillner *et al.*, "Antibodies against a synthetic peptide identify the Epstein-Barr virus-determined nuclear antigen," *Proc. Natl. Acad. Sci. USA* 81:4652-56 (1984) (attached hereto as Exhibit D).

---

[16] Office Action, page 7.

[17] Office Action, page 5.

The ease with which those skilled in the art can raise antibodies to peptides, polypeptides, and proteins of known sequence is indeed so well established that the Court of Appeals for the Federal Circuit recognizes that description of a polypeptide antigen's sequence is sufficient not only to *enable* the skilled artisan to prepare such antibodies, but also as a matter of law fully to *describe* such antibodies:

> based on our past precedent, as long as an applicant has disclosed a "fully characterized antigen," either by its structure, formula, chemical name, or physical properties, or by depositing the protein in a public depository, the applicant can then claim an antibody by its binding affinity to that described antigen. *Noelle v. Lederman*, 355 F.3d 1343, 1349 (Fed. Cir. 2004).

And it is of course not true that "the specification does not disclose an immunogenic fragment comprising at least 15 or 20 amino acids of SEQ.ID.NO:2"[18]: the full length BASB111 protein, agreed to be fully enabled, comprises each and every fragment of 15 contiguous amino acids, and each and every fragment of 20 contiguous amino acids.[19]

The Examiner does not suggest that antibodies with specificity for BASB111 cannot be used to detect *M. catarrhalis* or disease caused by *M. catarrhalis* . Rather, the Examiner posits that a global miasma of unpredictability in the field of "protein chemistry" somehow vitiates this clinical utility, at least so far as inclusion of immunogenic fragments within larger proteins, relying in part on citation to a 1976 treatise on peptide hormones.[20]

The Examiner's concern is at best misplaced.

---

[18] Office action, page 2.

[19] Given the purely mechanical nature of the task, it is not necessary that each such fragment encompassed within the disclosed sequence be written out to satisfy the written description requirement of section 112. *See*, *Capon v. Eshhar*, 76 USPQ2d 1078 (Fed. Cir. 2005).

[20] Office Action, page 5.

The fact that "replacement of a single lysine residue at position 118 of the acidic fibroblast growth factor by glutamic acid led to a substantial loss of heparin binding, receptor binding, and biological-activity of the protein",[21] while interesting, is inapposite to the issue here presented. The fact that "replacement of aspartic acid at position 47" of transforming growth factor alpha with "serine or glutamic acid sharply reduced the biologic activity of the mitogen" is irrelevant. We are not here speaking about the natural biological function of BASB111 in the lifecyle of the *M.catarrhalis* bacterium, but rather to the ease with which a BASB111 fragment can be used, in a fusion or a conjugate, to raise anti-*M. catarrhalis* antibodies, which can in turn be used to detect the bacterium in clinically relevant samples.

"[A] specification disclosure which contains a teaching of the manner and process of making and using the invention in terms which correspond in scope to those used in describing and defining the subject matter sought to be patented must be taken as in compliance with the enabling requirement of the first paragraph of § 112 unless there is reason to doubt the objective truth of the statements contained therein which must be relied on for enabling support." *In re Marzocchi*, 439 F.2d 220, 223 (CCPA 1971), quoted with approval in *In re Brana*, 51 F.3d 1560, 1566 (Fed. Cir. 1995).

If the Examiner has a credible reference that speaks to a routine loss of immunogenicity of an otherwise immunogenic fragment when conjugated to or fused within a larger polypeptide or protein, the relevant issue might then properly have been placed in contention. Absent such reference, however, the Examiner has not provided reason to doubt the objective truth of the statements in applicant's specification, and the Examiner's *prima facie* case fails. *In re Brana, Id.* ("Only after the PTO provides evidence showing that one of ordinary skill in the art would reasonably doubt the asserted utility does the burden shift to the applicant to provide rebuttal evidence sufficient to convince such a person of the invention's asserted utility."). Accordingly, the Examiner's rejection is in error, and should be withdrawn.

---

[21] Office Action, paragraph bridging pages 5 – 6.

Claims 44-45 and claim 28 (as vaccine composition only)

Claims 44-45 and claim 28 (as a vaccine composition only) stand rejected under 35 U.S.C. §112, first paragraph, for the same reasons as set forth in the previous action. Claims 28 and 44-45 have been cancelled[22] and replaced with new claims 63-67. Applicant traverses the rejection as it applies to new claims 63-67.

The Examiner contends that "applicant's specification does not disclose and there is no evidence of record that the claimed polypeptide/fragments would generate an immune response that one could use it for the treatment of otitis media or respiratory diseases. Further, as indicated above, the claimed uncharacterized antigens have not been shown to induce an immune response that could prevent the infection as the claimed invention is drawn to a vaccine composition."[23]

Applicant, in Example 5, describes the production of an *M. catarrhalis* bactericidal immune response using a vaccine comprising recombinant BASB111. In Example 8, the activities of pre-immune and anti-BASB111 antisera in mediating killing of *M. catarrhalis* are described. The bactericidal titer of rabbit and mouse antisera, as demonstrated by an *in vitro* assay, increased from < 1:60 (pre-immune) to > 1:316 (immune), which is greater than about a five-fold increase in bacterial killing. Thus, the disclosure is enabling for *M. catarrhalis* vaccines comprising BASB111 protein and fragments thereof.[24] Accordingly, the Examiner's rejection is in error, and should be withdrawn.

Rejection Under 35 U.S.C. § 102(b)

Claims 28, 30, 33, 35, 44, 45 and 51-54 stand rejected under 35 U.S.C. § 102(b) as being anticipated by Christensen et al., 1996, "Serum Antibody Response to Outer Membrane Proteins

---

[22] Hence the rejection is moot as applied to cancelled claims 28 and 44-45.

[23] Office Action, page 11.

[24] As discussed above, comprises each and every fragment of 40 contiguous amino acids.

of *Moraxella* (*Branhamella*) *catarrhalis* in Patients with Bronchopulmonary Infection," Clinical and Diagnostic Laboratory Immunology, 3(6):717-721 ("Christensen et al."). Claims 28, 30, 33, 35, 44, 45 and 51-54 have been cancelled[25] and replaced with new claims 55-67. Applicant traverses the rejection as it applies to new claims 55-67.

Claims 28, 30, 33 and 35

Christensen et al describe the outer membrane protein (OMP) patterns obtained by SDS-PAGE of seven *M. catarrhalis* strains. Approximately 25 bands with molecular masses of between 140 and 16 kDa were identified, with the principal protein components having molecular masses of 98, 84, 72, 69, 56, 43, 28 and 21 kDa.[26]

The Examiner posits that the 28 kDA polypeptide "appears to be same as the claimed polypeptide, SEQ.ID.NO:2 having 276 amino acids because molecular weight of an amino acid is approximately 110 daltons. Therefore, 28 kDA protein read (sic) on claims."[27]

In the present response, cancelled claims 28, 30, 33 and 35 are replaced by new claims 55-58, drawn to an isolated recombinant polypeptide of SEQ ID NO:2 and fragments of SEQ ID NO:2.

> "A patent is invalid for anticipation if a single prior art reference discloses ***each and every limitation*** of the claimed invention. Moreover, a prior art reference may anticipate without disclosing a feature of the claimed invention if that missing characteristic is ***necessarily present***, or inherent, in the single anticipating reference." *Schering Corp. v. Geneva Pharms., Inc.*, 339 F.3d 1373, 1377 (Fed. Cir. 2003) (discussing the standards for inherent anticipation; internal citations omitted; emphasis added) (quoted with approval in *SmithKline Beecham Corp. v. Apotex Corp.*, 403 F.3d 1331 (Fed. Cir. 2005)).

---

[25] Hence the rejection is moot as applied to cancelled claims 28, 30, 33, 35, 44, 45 and 51-54 .

[26] Christensen et al., page 718.

[27] Office Action, page 12.

Whether Christensen's OMP preparations "inherently comprise SEQ ID NO:2, [and] many fragments of SEQ ID NO:2 " – that is, whether "SEQ.ID.NO:2, [and] many fragments of SEQ.ID.NO:2" are "necessarily present", a contention as to which Applicant here offers no comment – OMP preparations from untransformed strains simply ***cannot*** contain the "***isolated recombinant*** polypeptide" of applicant's claims 55-58. Lacking explicit elements of applicant's claims, the OMP preparations cannot and do not anticipate these claims, either expressly or by inherency. With respect, the rejection is in error and should be withdrawn.

Claims 59-61

Applicant's claims 59-61, are drawn to "[a]n isolated recombinant fusion protein comprising the polypeptide" of earlier claims, fused to a second polypeptide moiety. The Examiner does not contend, nor plausibly could contend, that Christensen et al discloses an isolated fusion protein comprising SEQ ID NO:2 or fragments thereof.

The M.P.E.P. correctly describes the controlling jurisprudential standard for establishing anticipation of a claim:

> **TO ANTICIPATE A CLAIM, THE REFERENCE MUST TEACH EVERY ELEMENT OF THE CLAIM.**
>
> "A claim is anticipated only if each and every element as set forth in the claim is found, either expressly or inherently described, in a single prior art reference." *Verdegaal Bros. v. Union Oil. Co. of California*, 814 F.2d 628, 631, 2 USPQ2d 1051, 1053 (Fed. Cir. 1987). . . . "The identical invention must be shown in as complete detail as is contained in the . . . claim." *Richardson v. Suzuki Motor Co.*, 868 F.2d 1226, 1236, 9 USPQ2d 1913, 1920 (Fed. Cir. 1989). The elements must be arranged as required by the claim, but this is not an *ipsissimis verbis* test, i.e., identity of terminology is not required. *In re Bond*, 910 F.2d 831, 15 USPQ2d 1566 (Fed. Cir. 1990).

M.P.E.P. § 2131 (8th ed., rev. 2) (heading capitalization and font emphasis in the original).

Lacking the recombinant fusion protein of Applicant's claims, the cited reference cannot anticipate claims 59-61. With respect, the rejection is manifestly in error and should be withdrawn.

Claims 62-63

Claims 62-63 are drawn to immunogenic compositions.

With respect to the immunogenic compositions of claims 62-63, the Examiner posits that Christensen's "outer membrane preparations read on immunogenic composition as outer membrane proteins bind to the convalescent sera."[28]

Each of new claims 62-63, requires that the immunogenic composition comprise an isolated recombinant protein comprising at least an immunogenic fragment of BASB111. No such isolated recombinant protein is present in the outer membrane protein preparations of Christensen et al. Lacking such element, Christensen et al. cannot anticipate. The rejection is in error and should be withdrawn.

Claims 64-67

Claims 64-67 are drawn to vaccine compositions.

With respect to the vaccine compositions of claims 64-67, the Examiner posits that Christensen's "outer membrane protein preparations reads on a vaccine composition because vaccine is treated as intended use of said composition . . . As outer membrane protein contains several antigens in the preparation, it meets the limitation one other Moraxella antigen of claim 45."[29]

---

[28] Office Action, page 12.

[29] Office Action, page 12.

Each of new claims 64-67, requires that the vaccine composition comprise an isolated recombinant protein comprising at least an immunogenic fragment of BASB111. No such isolated recombinant protein is present in the outer membrane protein preparations of Christensen et al. Lacking such element, Christensen et al. cannot anticipate. The rejection is in error and should be withdrawn.

Claim 28(b) stands rejected under 35 U.S.C. § 102(b) as being anticipated by Murphy et al., 1993, Database: PIR_78, Accession number JN0751 ("Murphy et al."). Specifically, the Patent Office alleges that "Murphy et al disclose an isolated polypeptide comprising a fragment of at least 15 amino acids or 20 amino acids that matches 100% with an aligned contiguous segment of SEQ.ID.NO:2."[30] Claim 28b has been cancelled[31] and replaced with new claims 55b and 58. Applicant traverses the rejection as it applies to new claim 55b and 58.

Applicant submits that the rejection does not apply to new claim 55b, drawn to "an immunogenic fragment of at least 40 contiguous amino acids of SEQ ID NO:2; wherein the immunogenic fragment, when administered to a subject in a composition which can include an adjuvant, or conjugated to a suitable carrier, induces an antibody or T-cell immune response that recognizes the polypeptide SEQ ID NO:2" or to claim 59, drawn to "[t]he isolated recombinant polypeptide of claim 55, wherein the polypeptide comprises an immunogenic fragment of at least 40 contiguous amino acids of SEQ ID NO:2; wherein the immunogenic fragment, when administered to a subject in a composition which can include an adjuvant, or conjugated to a suitable carrier, induces an antibody or T-cell immune response that recognizes the polypeptide SEQ ID NO:2.

Referring to the sequence alignment run by the Examiner in the Office Action mailed August 16, 2004, Applicant submits that Murphy et al. do not disclose an isolated polypeptide

---

[30] Office Action, page 14.

[31] Hence the rejection is moot as applied to cancelled claim 28b.

comprising a fragment of at least 40 amino acids that matches 100% with an aligned contiguous segment of SEQ.ID.NO:2.

> "A patent is invalid for anticipation if a single prior art reference discloses ***each and every limitation*** of the claimed invention. Moreover, a prior art reference may anticipate without disclosing a feature of the claimed invention if that missing characteristic is ***necessarily present***, or inherent, in the single anticipating reference." *Schering Corp. v. Geneva Pharms., Inc.*, 339 F.3d 1373, 1377 (Fed. Cir. 2003) (discussing the standards for inherent anticipation; internal citations omitted; emphasis added) (quoted with approval in *SmithKline Beecham Corp. v. Apotex Corp.*, 403 F.3d 1331 (Fed. Cir. 2005)).

Accordingly, Murphy et al do not disclose a fragment of at least 40 contiguous amino acids that is identical to a corresponding fragment in SEQ ID NO:2. Lacking this element of new claims 55b and 58, the reference cannot anticipate and should be withdrawn.

Conclusion

Claims 55-68 are believed to satisfy all of the criteria for patentability and are in condition for allowance. An early indication of the same is therefore kindly requested.

No fees beyond those submitted herewith are believed to be due in connection with this Amendment. However, the Commissioner is authorized to charge any additional fees that may required, or credit any overpayment, to Dechert LLP Deposit Account No. 50-0258 (Order No. BM45395 (306550).

Respectfully submitted,

Date: November 12, 2005

Renee M. Kosslak
Reg. No. 47,717

DECHERT LLP
Customer No. 37509
Telephone: 650.813.4800
Facsimile: 650.813.4848

Attachments:

Exhibit A: Niman *et al.*, *Proc. Natl. Acad. Sci. USA* 80:4949-4953 (1983)

Exhibit B: Shinnick *et al.*, *Ann. Rev. Microbiol.* 37:426-26 (1983)

Exhibit C: Geysen *et al.*, *Proc. Natl. Acad. Sci. USA* 82:178-82 (1985)

Exhibit D: Dillner *et al.*, *Proc. Natl. Acad. Sci. USA* 81:4652-56 (1984)

11910920.BUSINESS